

RESPONSE TO RESTRICTION REQUIREMENT

3. (Amended) A method as claimed in Claim 1, wherein the [ligands in the mixture are immobilized] mixture of ligands is separated on the basis of one or more parameters before it is exposed to the library.

4. (Amended) A method as claimed in Claim [1] 3, wherein the mixture of ligands is separated [on the basis of one or more parameters before it is exposed to the library] using two-dimensional gel electrophoresis.

5. (Amended) A method as claimed in Claims 4 wherein the [mixture of] ligands [is separated using two-dimensional gel electrophoresis] in the separated mixture are immobilized on a support surface.

6. (Amended) A method as claimed in Claim 5, wherein the [ligands in the separated are immobilized on a] support surface is a nitrocellulose or polyvinylidene difluoride (PVDF) membrane.

7. (Amended) A method as claimed in Claim [6] 5 wherein the support surface is a [nitrocellulose or polyvinylidene difluoride (PVDF) membrane] replica of the two dimensional gel and is used directly in step (iii) of the method of Claim 1.

~~8. (Amended) A method as claimed in Claim [6] 1, wherein the [support surface is a replica of the two-dimensional gel and is used directly in step (iii) of the method of Claim 1] anti-ligand comprises a protein or polypeptide.~~

~~9. (Amended) A method as claimed in Claim [2] 8 wherein the [ligands in the mixture are tagged by a tagging agent so that they can be isolated by an anti-tagging agent which binds to the tagging agent] anti-ligand is an antibody or an antigen binding variant or derivative thereof.~~

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10. (Amended) A method as claimed in Claim [9] 1 wherein the [tagging agent is biotin and the anti-tagging agent is avidin] anti-ligand is a nucleic acid.

11. (Amended) A method as claimed in claim 1 wherein the [anti-ligand comprises a protein or polypeptide] identity of at least some of the ligands and/or anti-ligands is unknown.

12. (Amended) A method as claimed in Claim 11 wherein the [anti-ligand is an antibody or an antigen binding variant or derivative thereof] identity of substantially all of the ligands and/or anti-ligands is unknown.

13. (Amended) A method as claimed in claim 1 wherein [the anti-ligand is a nucleic acid] 10 to 50 different anti-ligands are applied per region of the array.

Please cancel claims 14-26.

27. (New) A method of isolating ligands comprising

- (i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;
- (ii) providing one or more compounds to be screened as ligands;
- (iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;
- (iv) isolating the compounds which bind to the anti-ligands.

28. (New) A method comprising providing an array made by a method comprising

- (i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

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(ii) providing one or more compounds to be screened as ligands; and

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

further comprising

comparing the presence, absence and/or amount of one or more ligands in first and second biological samples by detecting differences in ligand/anti-ligand binding when the array is exposed to the samples.

29. (New) A method comprising providing an array made by a method comprising

(i) providing a library of anti-ligand molecules displayed for binding with a ligand on the surface of one or more replicable units;

(ii) providing one or more compounds to be screened as ligands; and

(iii) exposing the compounds to the library of anti-ligand molecules whereby ligand/anti-ligand binding can take place;

comprising comparing the presence, absence and/or amount of one or more ligands in first and second biological samples by detecting differences in ligand/anti-ligand binding when an array is exposed to the first biological sample and a substantially identical array is exposed to the second biological sample.

30. (New) A method as claimed in Claim 28 wherein the ligands in the first and second biological samples are labeled with different first and second fluorescent reporters so that, in use, under examination of the array under conditions of fluorescence excitation, anti-ligands in the array which are bound predominantly to ligands from one of the first and second

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biological samples give a first or second fluorescence emission; and anti-ligands which bind substantially equal numbers of ligands from the first and second biological samples give a combined fluorescence emission.

31. (New) A method as claimed in Claim 29 wherein the ligands in the first and second biological samples are labeled with different first and second fluorescent reporters so that, in use, under examination of the array under conditions of fluorescence excitation, anti-ligands in the array which are bound predominantly to ligands from one of the first and second biological samples give a first or second fluorescence emission; and anti-ligands which bind substantially equal numbers of ligands from the first and second biological samples give a combined fluorescence emission.

32. (New) A method as claimed in Claim 28 wherein the first and second biological samples are applied to identical but separate arrays of anti-ligands.

33. (New) A method as claimed in Claim 29 wherein the first and second biological samples are applied to identical but separate arrays of anti-ligands.

34. (New) A method as claimed in Claim 28 wherein the mixture of ligands provided in step (ii) of the method of making the array is derived from the same source as the first or second biological sample.

35. (New) A method as claimed in Claim 29 wherein the mixture of ligands provided in step (ii) of the method of making the array is derived from the same source as the first or second biological sample.